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CLAIMS

1. A compound of the formula

$$R^3$$
 R^2
 R^4
 R^2

wherein phenyl ring A and phenyl ring B can each, independently, be replaced by a naphthyl group, and wherein when phenyl ring A is replaced by a naphthyl group, the ethereal oxygen of structure I and the carbon to which R³, R⁴ and NR¹R² are attached, are attached to adjacent ring carbon atoms of the naphthyl group and neither of said adjacent ring carbon atoms is also adjacent to a fused ring carbon atom of said naphthyl group;

n and m are, selected, independently, from one, two and three;

 R^1 and R^2 are selected, independently, from hydrogen, (C_1-C_4) alkyl, (C_2-C_4) alkenyl, and (C_2-C_4) alkynyl, or R^1 and R^2 , together with the nitrogen to which they are attached, form a four to eight membered saturated ring containing one or two heteroatoms, including the nitrogen to which R^1 and R^2 are attached, wherein the second heteroatom, when present, is selected from oxygen, nitrogen and sulfur, and wherein said ring may optionally be substituted at available binding sites with from one to three substituents selected, independently, from hydroxy and (C_1-C_6) alkyl;

 R^3 and R^4 are selected, independently, from hydrogen and (C_1-C_4) alkyl optionally substituted with from one to three fluorine atoms, or R^3 and R^4 , together with the carbon to which they are attached, form a four to eight membered saturated carbocyclic ring, and wherein said ring may optionally be substituted at available binding sites with from one to three substituents selected, independently, from hydroxy and (C_1-C_6) alkyl;

or R^2 and R^3 , together with the nitrogen to which R^2 is attached and the carbon to which R^3 is attached, form a four to eight membered saturated ring containing one or two heteroatoms, including the nitrogen to which R^2 is attached, wherein the second heteroatom, when present, is selected from oxygen, nitrogen and sulfur, and wherein said ring may optionally be substituted at available binding sites with from one to three substituents selected, independently, from hydroxy and (C_1-C_6) alkyl;

each X is selected, independently, from hydrogen, halo (<u>i.e.</u>, chloro, fluoro, bromo or iodo), (C₁-C₄)alkyl optionally substituted with from one to three fluorine atoms, (C₁-C₄)alkoxy USERS\DOCS\LA21952\LPKXD\2RM\$01!.DOC/129114/PC10434.NEW.KXD



optionally substituted with from one to three fluorine atoms, cyano, nitro, amino, (C1-C₄)alkylamino, di-[(C₁-C₄)alkyl]amino, NR⁵(C=O)(C₁-C₄)alkyl, SO₂NR⁵R⁶ and SO_p(C₁-C₆)alkyl, wherein R⁵ and R⁶ are selected, independently, from hydrogen and (C₁-C₆)alkyl, and p is zero, one or two; and

each Y is selected, independently, from hydrogen, (C1-C6)alkyl and halo;

with the proviso that: (a) no more than one of NR¹R², CR³R⁴ and R²NCR³ can form a ring; and (b) at least one X must be other than hydrogen when (i) R3 and R4 are both hydrogen, (ii) R¹ and R² are selected, independently, from hydrogen and (C₁-C₄)alkyl, and (iii) ring B is mono- or disubstituted with, respectively, one or two halo groups;

or a pharmaceutically acceptable salt thereof.

- A compound or salt according to claim1, wherein n is one, X is fluoro, R3 and 2. R^4 are hydrogen, R^1 is hydrogen, R^2 is methyl, m is two and Y is Y_m is 3,4-dichloro.
- A compound or salt according to claim 1, wherein m is zero, n is one, R3 and R⁴ are hydrogen, X is chloro, bromo, iodo or methyl, R¹ is hydrogen and R² is methyl.
- A compound or salt according to claim 1, wherein said compound or salt is selected from the following compounds and their pharmaceutically acceptable salts:

[2-(3,4-Dichlorophenoxy)-5-fluorobenzyl]-dimethylamine;

[2-(3,4-Dichlorophenoxy)-5-fluorobenzyl]-methylamine;

[2-(3,4-Dichlorophenoxy)-5-trifluoromethylbenzyl]-dimethylamine;

N-[4-(3,4-Dichlorophenoxy)-3-dimethylaminomethylphenyl]-acetamide; 20

{1-[2-(3,4-Dichlorophenoxy)phenyl]-ethyl}-dimethylamine;

[2-(3,4-Dichlorophenoxy)-4-trifluoromethylbenzyl]-dimethylamine;

[2-(3,4-Dichlorophenoxy)-4-trifluoromethylbenzyl]-methylamine;

[4-Chloro-2-(3,4-dichlorophenoxy)-benzyl]-methylamine;

{1-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-ethyl}-methylamine; 25

{1-[2-(3,4-Dichlorophenoxy)phenyl}-ethyl}-methylamine;

{1-[2-(4-Chlorophenoxy)phenyl]ethyl}-methylamine;

[2-(3,4-Dichlorophenoxy)-5-methoxybenzyl]-methylamine;

[2-(4-Chlorophenoxy)-5-fluorobenzyl]-methylamine;

{1-[2-(4-Chlorophenoxy)-5-fluorophenyl]-ethyl}-methylamine; 30

[2-(3,4-Dichlorophenoxy)-5-methylbenzyl]-dimethylamine;

[4-Bromo-2-(3,4-dichlorophenoxy)-benzyl]-methylamine;

[5-Bromo-2-(3,4-dichlorophenoxy)-benzyl]-methylamine;

[2-(3,4-Dichlorophenoxy)-4,5-dimethoxybenzyl]-methylamine;

[2-(3,4-Dichlorophenoxy)-4-methoxybenzyl]-dimethylamine;

4-(3,4-Dichlorophenoxy)-3-methylaminomethyl-benzonitrile;

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[2-(3,4-Dichlorophenoxy)-4,5-dimethylbenzyl]-methylamine; 3-(3,4-Dichlorphenoxy)-4-methylaminomethyl-benzonitrile;

(+)-{1-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-ethyl}-methylamine;

(-)-{1-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-ethyl}-methylamine;

[2-(3,4-Dichlorophenoxy)-5-trifluoromethyl-benzyl]-methylamine;

[2-(3,4-Dichlorophenoxy)-4-methoxybenzyl]-methylamine;

[2-(4-Chloro-3-fluorophenoxy)-5-fluorobenzyl]-methylamine;

[2-(3-Chloro-4-fluorophenoxy)-5-fluorobenzyl]-methylamine;

(+/-)-2-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-pyrrolidine;

(-)-2-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-pyrrolidine;

(+)-2-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-pyrrolidine; and

2-[2-(3,4-Dichlorophenoxy)-5-fluorophenyl]-N-methylpyrrolidine;

- A pharmaceutical composition for treating a disorder or condition selected from hypertension, depression (e.g., depression in cancer patients, depression in Parkinson's patients, postmyocardial infarction depression, subsyndromal symptomatic depression, depression in infertile women, pediatric depression, major depression, single episode depression, recurrent depression, child abuse induced depression, and post partum depression), generalized anxiety disorder, phobias (e.g., agoraphobia, social phobia and simple phobias), posttraumatic stress syndrome, avoidant personality disorder, premature ejaculation, eating disorders (e.g., anorexia nervosa and bulimia nervosa), obesity, chemical dependencies (e.g., addictions to alcohol, cocaine, heroin, phenobarbital, nicotine and benzodiazepines), cluster headache, migraine, pain, Alzheimer's disease, obsessivecompulsive disorder, panic disorder, memory disorders (e.g., dementia, amnestic disorders, and age-related cognitive decline (ARCD)), Parkinson's diseases (e.g., dementia in Parkinson's disease, neuroleptic-induced parkinsonism and tardive dyskinesias), endocrine disorders (e.g., hyperprolactinaemia), vasospasm (particularly in the cerebral vasculature), cerebellar ataxia, gastrointestinal tract disorders (involving changes in motility and secretion), negative symptoms of schizophrenia, premenstrual syndrome, fibromyalgia syndrome, stress incontinence, Tourette's syndrome, trichotillomania, kleptomania, male impotence, attention deficit hyperactivity disorder (ADHD), chronic paroxysmal hemicrania and headache (associated with vascular disorders) in a mammal, preferably a human, comprising an amount of a compound according to claim 1 that is effective in treating such disorder or condition and a pharmaceutically acceptable carrier.
- 6. A pharmaceutical composition for treating a disorder or condition that can be treated by inhibiting the reuptake of serotonin, dopamine or norepinephrine in a mammal,

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preferably a human, comprising an amount of a compound according to claim 1 that is effective in treating such disorder or condition and a pharmaceutically acceptable carrier.

- 7. A method for treating a disorder or condition selected from hypertension, depression (e.g., depression in cancer patients, depression in Parkinson's patients, postmyocardial infarction depression, subsyndromal symptomatic depression, depression in infertile women, pediatric depression, major depression, single episode depression, recurrent depression, child abuse induced depression, and post partum depression), generalized anxiety disorder, phobias (e.g., agoraphobia, social phobia and simple phobias), posttraumatic stress syndrome, avoidant personality disorder, premature ejaculation, eating disorders (e.g., anorexia nervosa and bulimia nervosa), obesity, chemical dependencies (e.g., addictions to alcohol, cocaine, heroin, phenobarbital, nicotine and benzodiazepines), cluster headache, migraine, pain, Alzheimer's disease, obsessive-compulsive disorder, panic disorder, memory disorders (e.g., dementia, amnestic disorders, and age-related cognitive decline (ARCD)), Parkinson's diseases (e.g., dementia in Parkinson's disease, neuroleptic-induced parkinsonism and tardive dyskinesias), endocrine disorders (e.g., hyperprolactinaemia), vasospasm (particularly in the cerebral vasculature), cerebellar ataxia, gastrointestinal tract disorders (involving changes in motility and secretion), negative symptoms of schizophrenia, premenstrual syndrome, fibromyalgia syndrome, stress incontinence, Tourette's syndrome, trichotillomania, kleptomania, male impotence, attention deficit hyperactivity disorder (ADHD), chronic paroxysmal hemicrania and headache (associated with vascular disorders) in a mammal, comprising administering to a mammal in need of such treatment an amount of a compound according to claim 1 that is effective in treating such disorder or condition.
- 8. A method for treating a disorder or condition that can be treated by inhibiting the reuptake of serotonin, dopamine or norepinephrine in a mammal, comprising administering to a mammal in need of such treatment an amount of a compound according to claim-1 that is effective in treating such disorder or condition.
- 9. A pharmaceutical composition for treating a disorder or condition selected from hypertension, depression (e.g., depression in cancer patients, depression in Parkinson's patients, postmyocardial infarction depression, subsyndromal symptomatic depression, depression in infertile women, pediatric depression, major depression, single episode depression, recurrent depression, child abuse induced depression, and post partum depression), generalized anxiety disorder, phobias (e.g., agoraphobia, social phobia and simple phobias), posttraumatic stress syndrome, avoidant personality disorder, premature ejaculation, eating disorders (e.g., anorexia nervosa and bulimia nervosa), obesity, chemical dependencies (e.g., addictions to alcohol, cocaine, heroin, phenobarbital, nicotine and benzodiazepines), cluster headache, migraine, pain, Alzheimer's disease, obsessive-

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compulsive disorder, panic disorder, memory disorders (e.g., dementia, amnestic disorders, and age-related cognitive decline (ARCD)), Parkinson's diseases (e.g., dementia in Parkinson's disease, neuroleptic-induced parkinsonism and tardive dyskinesias), endocrine disorders (e.g., hyperprolactinaemia), vasospasm (particularly in the cerebral vasculature), cerebellar ataxia, gastrointestinal tract disorders (involving changes in motility and secretion), negative symptoms of schizophrenia, premenstrual syndrome, fibromyalgia syndrome, stress incontinence, Tourette's syndrome, trichotillomania, kleptomania, male impotence, attention deficit hyperactivity disorder (ADHD), chronic paroxysmal hemicrania and headache (associated with vascular disorders) in a mammal, comprising a serotonin, dopamine or norepinephrine reuptake inhibiting effective amount of a compound of the formula I, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

- 10. A pharmaceutical composition for treating a disorder or condition that can be treated by inhibiting the reuptake of serotonin, norepinephrine or dopamine in a mammal, comprising serotonin, dopamine or norepinephrine reuptake inhibiting effective amount of a compound according to claim *\frac{1}{2}\$ and a pharmaceutically acceptable carrier.
- A method for treating a disorder or condition selected from hypertension, 11. depression (e.g., depression in cancer patients, depression in Parkinson's patients, postmyocardial infarction depression, subsyndromal symptomatic depression, depression in infertile women, pediatric depression, major depression, single episode depression, recurrent depression, child abuse induced depression, and post partum depression), generalized anxiety disorder, phobias (e.g., agoraphobia, social phobia and simple phobias), posttraumatic stress syndrome, avoidant personality disorder, sexual dysfunction (e.g., premature ejaculation), eating disorders (e.g., anorexia nervosa and bulimia nervosa), obesity, chemical dependencies (e.g., addictions to alcohol, cocaine, heroin, phenobarbital, nicotine and benzodiazepines), cluster headache, migraine, pain, Alzheimer's disease, obsessivecompulsive disorder, panic disorder, memory disorders (e.g., dementia, amnestic disorders, and age-related cognitive decline (ARCD)), Parkinson's diseases (e.g., dementia in Parkinson's disease, neuroleptic-induced parkinsonism and tardive dyskinesias), endocrine disorders (e.g., hyperprolactinaemia), vasospasm (particularly in the cerebral vasculature), cerebellar ataxia, gastrointestinal tract disorders (involving changes in motility and secretion), negative symptoms of schizophrenia, premenstrual syndrome, fibromyalgia syndrome, stress incontinence, Tourette's syndrome, trichotillomania, kleptomania, male impotence, attention deficit hyperactivity disorder (ADHD), chronic paroxysmal hemicrania and headache (associated with vascular disorders) in a mammal, preferably a human, comprising administering to a mammal requiring such treatment a serotonin, dopamine or norepinephrine

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reuptake inhibiting effective amount of a compound according to claim 1 or a pharmaceutically acceptable salt thereof.

- 12. A method for treating a disorder or condition that can be treated by inhibiting the reuptake of serotonin, norepinephrine or dopamine in a mammal, comprising administering to a mammal requiring such treatment a serotonin, dopamine or norepinephrine reuptake inhibiting effective amount of a compound according to claim 1.
- 13. A pharmaceutical composition for treating a condition or disorder that can be treated by inhibiting the reuptake of serotonin, dopamine or norepinephrine in a mammal, comprising:
- a) a pharmaceutically acceptable carrier;
 - b) a compound according to claim 1; and
 - c) an NK-1 receptor antagonist or a 5HT_{1D} receptor antagonist, or a pharmaceutically acceptable salt thereof;

wherein the amount of the active compounds (<u>i.e.</u>, the compound of formula I and the NK-1 receptor antagonist or 5HT_{1D} receptor antagonist) are such that the combination is effective in treating such disorder or condition.

- 14. A method for treating a disorder or condition that can be treated by inhibiting the reuptake of serotonin, dopamine or norepinephrine in a mammal, comprising administering to a mammal requiring such treatment:
 - a) a compound according to claim 4; and
- b) an NK-1 receptor antagonist or 5HT_{1D} receptor antagonist, or a pharmaceutically acceptable salt thereof;

wherein the amounts of the active compounds (i.e., the compound of formula I and the NK-1 receptor antagonist or 5HT_{1D} receptor antagonist) are such that the combination is effective in treating such disorder or condition.

15. A compound of the formula

wherein Q is -C(=O)H, cyano, -C(=O)OH, or -C(=O)NR¹R² wherein R¹ and R² are selected, independently, from hydrogen and (C₁-C₄)alkyl, or R¹ and R², together with the nitrogen to USERS\DOCS\LA21952\LPKXD\ZRM\$01!.DOC/129114/PC10434.NEW.KXD

which they are attached, form a four to eight membered saturated ring containing one or two heteroatoms, including the nitrogen to which R¹ and R² are attached, wherein the second heteroatom, when present, is selected from oxygen, nitrogen and sulfur.